Published in final edited form as:

Am J Clin Oncol. 2018 July ; 41(7): 626–631. doi:10.1097/COC.0000000000000339.

Clinical and economic evaluation of treatment strategies for T1N0 anal canal cancer

Ashish A. Deshmukh, Ph.D., M.P.H.¹, Hui Zhao, Ph.D.², Prajnan Das, M.D., M.S., M.P.H.³, Elizabeth Y. Chiao, M.D., M.P.H.⁴, Yi-Qian Nancy You, M.D., M.H.Sc., F.A.C.S.⁵, Luisa Franzini, Ph.D.⁶, David R. Lairson, Ph.D.⁷, Michael D. Swartz, Ph.D.⁷, Sharon H. Giordano, M.D., M.P.H.², and Scott B. Cantor, Ph.D.²

¹ Department of Health Services Research, Management and Policy, University of Florida, Gainesville, Florida

² Department of Health Services Research, The University of Texas MD Anderson Cancer Center, Houston, Texas

³ Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas

⁴ Department of Medicine, Section of Infectious Disease, Baylor College of Medicine, Houston, Texas

⁵ Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas

⁶ Department of Health Services Administration, University of Maryland School of Public Health

⁷ The University of Texas Health Science Center of Houston School of Public Health

Abstract

Objective—A comparative assessment of treatment alternatives for T1N0 anal canal cancer has never been conducted. We compared the outcomes associated with the treatment alternatives—chemoradiotherapy (CRT), radiotherapy (RT), and surgery or ablation techniques (surgery/ablation)—for T1N0 anal canal cancer.

Methods—This retrospective cohort study was conducted using the Surveillance, Epidemiology and End Results (SEER) registries linked with Medicare longitudinal data (SEER-Medicare database). Analysis included 190 patients who were treated for T1N0 anal canal cancer using surgery/ablation [n = 44], radiotherapy (RT) [n = 50], or chemoradiotherapy (CRT) [n = 96]. The outcomes were reported in terms of survival and hazards ratios using Kaplan-Meier and Cox proportional hazards modeling, respectively; lifetime costs; and cost-effectiveness measured in terms of incremental cost-effectiveness ratio (ICER), i.e., the ratio of the difference in costs between the two alternatives to the difference in effectiveness between the same two alternatives.

Address correspondence and request for reprints to: Scott B. Cantor, Ph.D., Department of Health Services Research, Unit 1444, The University of Texas MD Anderson Cancer Center, P. O. Box 301402, Houston, TX 77230-1402, Phone: (713) 563-0020, FAX: (713) 563-0059, sbcantor@mdanderson.org.

Conflict of interest: None

Results—There was no significant difference in the survival duration between the treatment groups as predicted by the Kaplan-Meier curves. After adjusting for patient characteristics and propensity score, the hazard ratio of death for the patients who received CRT compared to surgery/ablation was 1.742 (95% CI 0.793 – 3.829) and RT was 2.170 (95% CI 0.923 – 5.101); however, the relationship did not reach statistical significance. Surgery/ablation resulted in lower lifetime cost than RT or CRT. The ICER associated with CRT compared to surgery/ablation was \$142,883 per life year gained.

Conclusion—There was no statistically significant difference in survival amongst the treatment alternatives for T1N0 anal canal cancer. Given that surgery/ablation costs less than RT or CRT and might be cost-effective compared with RT and CRT, it is crucial to explore this finding further in this era of limited health care resources.

Keywords

Anal cancer; T1N0; Stage I; Outcomes; Cost-effectiveness; Survival

INTRODUCTION

The incidence rates for anal canal cancer in the United States have doubled over the past 10 years.¹ If diagnosed and treated early, i.e., at stage T1N0 (when the tumor is < 2 cm in diameter (T1) with no regional lymph node metastasis (N0)), anal canal cancer has an observed 5-year patient survival rate of approximately 71%, compared to lower 5-year observed survival (approximately 50%) for tumors larger than 5 cm across.² Tumors less than 2 cm in diameter are curable in approximately 90% of the cases, whereas tumors larger than 5 cm are curable in fewer than 80% of the cases.^{3,4}

T1N0 anal canal cancer is typically treated with radiotherapy (RT), chemoradiotherapy (CRT), or surgery or ablation techniques such as cryosurgery (this will be referred to as “surgery/ablation” throughout the paper). Several randomized clinical trials (RCTs) have shown the benefits of CRT over RT; however, none of those studies focused specifically on T1N0 anal canal cancer.⁵⁻⁹ Some studies, mostly retrospective, have shown that external-beam RT alone, brachytherapy alone, or a combination of the two, is efficacious for T1N0 cancer.¹⁰⁻¹² Other studies have suggested CRT for the management of early-stage anal canal cancer.¹³ A study by Klas et al. showed that in patients treated for T1N0 anal cancer, CRT offered outcomes equivalent to those achieved with surgery-only therapy.¹⁴ In addition to these equivocal reports for CRT and RT, the outcomes associated with surgery/ablation for T1N0 tumors have never been evaluated in a clinical trial. According to the National Comprehensive Cancer Network (NCCN) guidelines, CRT is currently the primary therapy and standard of care for T1N0 anal canal cancer.¹⁵ Yet, no rationale for the use of CRT in these patients is provided in the guidelines. Given that CRT has associated side effects, RT or surgery/ablation may be associated with fewer long term side effects and yield better overall outcomes in these patients.

Uncertainty regarding the optimal treatment options for T1N0 anal canal cancer provides a strong rationale for comparing the outcomes for these treatment strategies. Moreover, economic outcomes including cost-effectiveness can be an important consideration in the

treatment selection process. Therefore, the purpose of this study was to evaluate the clinical outcomes, in terms of survival, associated with CRT, RT, and surgery/ablation for T1N0 anal canal cancer. Furthermore, we estimated the cost-effectiveness of treatment alternatives for these patients from a payer perspective.

MATERIAL AND METHODS

Data source and cohort identification

We conducted a retrospective cohort analysis using the Surveillance, Epidemiology and End Results (SEER) registries that collect demographic, and cause-of death information for patients with cancer and Medicare longitudinal data, with claims for all covered fee-for-service health care from the time of eligibility to death. The SEER-Medicare database is the result of the linkage of two large population-based sources of data: cancer registry data from the National Cancer Institute's sponsored cancer registries (SEER program) and Medicare claims from the Center for Medicare and Medicaid Services (CMS). Additional details of the SEER-Medicare database have been documented elsewhere.¹⁶

Patients diagnosed with T1N0 anal canal cancer between January 1, 1992, and December 31, 2009, were included in our study. We identified these patients using the ICD-O-3 site code of C21.0, C21.1, and C21.8 for anus, anal canal, and anorectum. The patients with anal margin tumor (ICD-O-3 code C44.5) were not included in this study. To identify patients with T1N0 anal cancer, the American Joint Committee on Cancer classification of malignant tumors (i.e., tumor, node, metastasis staging) was not available in the SEER data for the patients diagnosed between 1992 and 2004. A T1N0 stage variable for those patients was created using (1) information on the size of the primary tumor, (2) extent of spread to nearby lymph nodes, and (3) tumor metastasis to other organs of the body.

The study population was limited to patients age 66 years or older who had been diagnosed with pathologically confirmed anal cancer between 1992 and 2009 in SEER-linked Medicare database. The data were limited to patients older than 66 years to allow for a one-year period after Medicare enrollment (age 65 years) during which comorbidities could be recorded in claims files for the period before cancer diagnosis. Patients with unknown diagnosis months or diagnosis at autopsy or by death certificate only, or death date mismatch by SEER and Medicare datasets were excluded. We also identified noncancer cohort from the SEER-Medicare database, these were the patients identified from a 5% sample of Medicare beneficiaries. These patients were identified to estimate cancer-related costs. The detailed patient selection algorithm is presented in Figure 1.

The institutional review boards at The University of Texas MD Anderson Cancer Center and The University of Texas Health Science Center at Houston considered this research activity exempt and a waiver for informed consent was approved.

Patient Selection and treatment identification

The inclusion criteria for the study were (1) patients must have been 66 years or older and enrolled in Medicare at the time of diagnosis, (2) must have had continuous parts A and B coverage during the entire observation period, and (3) must have had histologically

confirmed anal cancer. We excluded the patients (1) if they were enrolled in Medicare managed care, and (2) if they were diagnosed only at death or if the month of their diagnosis was unknown.

After applying our inclusion and exclusion criteria, we identified 190 patients who received primary treatment for T1N0 anal canal cancer. As the purpose of the analysis was to identify first-line therapy (as opposed to therapy for tumor progression or tumor recurrence), initial treatment was defined using Medicare administrative codes for surgery (i.e., local excision) or ablation (for example, cryosurgery, laser surgery), RT, and CRT posted in the billing records within 180 days after the time of diagnosis. Using the Current Procedural Terminology (CPT) codes associated with the treatment alternatives, we identified patients treated with surgery/ablation, RT, or CRT (detailed treatment selection codes are provided in the Appendix).

Treatment effectiveness

Treatment effectiveness was defined in terms of survival duration from date of initial diagnosis.

Cost estimation

We used the Medicare payer perspective to estimate the treatment costs for each patient by adding the amounts reimbursed by Medicare beginning from the date of receipt of treatment to death. Total costs of care were estimated as the sum of Medicare payments for cancer-related care claims for health care services. The cancer-related costs were estimated by subtracting the costs for the non-cancer cohort from the costs for the cancer cohort. All costs were adjusted to the 2014 dollar amount using Medicare adjustment factors.¹⁷ A separate set of adjustment factors were used to adjust the costs for Medicare Part A and Part B.

For cancer-related cost estimation, we matched cancer patients with the non-cancer cohort by age and gender by assigning the same index date (i.e., both cases and controls were monitored from the date of cancer detection until their death or the end of Medicare claims)

Statistical analysis

Univariate analysis—For the purpose of univariate analysis, the chi-square test was used to compare the demographic and clinical characteristics among the patients who received surgery/ablation, RT, or CRT for T1N0 anal canal cancer.

Survival analysis: The purpose of the survival analysis was to compare overall survival stratified by treatments. Overall survival duration was defined as the time from the cancer diagnosis date until the patient's death. We censored the outcome data for the patients who were still alive at the end of follow-up period. We created Kaplan-Meier survival curves to compare survival duration following different primary treatments (surgery/ablation, RT, or CRT) among the study patients. We used the log-rank test to compare unadjusted survival rate. A parametric regression model was used to model survival. This model assumed that the median survival time followed the Weibull distribution, using age and sex as independent variables to predict the median survival time.¹⁸ A predictive equation was then derived from

the model to estimate the patients' life expectancy. In addition, we compared survival by treatment strategies using the Cox proportional hazards model, controlling for demographic and clinical explanatory variables, using the propensity score adjustment method.¹⁹ A propensity score is a measure of the likelihood of a subject's being assigned to a particular treatment group conditional on observed baseline characteristics.¹⁹ It has been reported in the literature that the adjustment using a propensity score mitigates the bias of the background covariates and may also control for biases introduced by unknown or unmeasured covariates associated with measured factors.²⁰ For propensity adjustment, we used covariate adjustment using propensity scores.²¹ Using this approach, the outcome variable was regressed on an indicator variable denoting treatment status and the estimated propensity score. For this, we selected a logistic regression model. The effect of treatment (adjusted odds ratio) was determined using the estimated regression coefficient from the fitted regression model. We adjusted for the covariates—age at diagnosis, marital status, geographic location of residence, and comorbidity in the logistic regression model. We reported the hazard ratios with two-sided p-values and 95% confidence intervals.

Cost-effectiveness analysis and uncertainty analysis—Costs and cost effectiveness were estimated by calculating the mean for each treatment strategy. The incremental cost-effectiveness ratio (ICER) $\frac{\Delta Cost}{\Delta Effectiveness}$ was estimated to evaluate the relative value of a given treatment to the next less costly alternative. Confidence intervals for the ICERs were generated using the net benefit regression approach.^{22,23} All future costs and outcomes were discounted using a discount rate of 3%.

RESULTS

Patient characteristics

A univariate analysis of patient demographic and clinical characteristics by treatment group is presented in Table 1. Of 190 patients, 44 (23.16%) were treated surgically, 96 (50.53%) patients received CRT, and 50 (26.32%) received RT only. The proportion of female patients in the study cohort was higher than the proportion of male patients. The proportion of white and married patients in the study cohort was higher than that of non-white and unmarried patients. Geographically, the Southwest region had a higher percentage of T1N0 anal canal cancer patients than the Midwest and Northeast regions.

Survival analysis

There was no significant difference in overall survival between the treatment groups as predicted by the Kaplan-Meier curves (log rank test, $p = 0.3186$). (See Figure 2.) In the unadjusted Cox proportional hazards model, the hazard ratio of death for patients who received CRT was 1.433 (95% CI 0.675 – 3.042) and those who received RT was 1.836 (95% CI 0.824 – 4.093) compared to the patients who were treated using surgery/ablation (Table 2); however, this relationship did not reach statistical significance. When adjusted for patient demographics and characteristics, the hazard ratio of death for the patients who received CRT was 1.168; 95% CI 0.768 – 3.623), and that for the patient who received RT was 2.075 (95% CI 0.895 – 4.811) than the patients who were treated using surgery/ablation.

When adjusted for propensity scores, the results changed slightly. However, none of these relationships reached statistical significance.

Cost-effectiveness analysis

The results of the cost-effectiveness analysis are presented in Table 3. In our study cohort, the mean cost associated with surgery/ablation was \$29,210, far less than the average costs associated with CRT (mean cost \$46,350) or RT only (mean cost \$49,400). CRT was associated an average survival of 7.72 years, followed by surgery/ablation (7.60 years) and RT (7.08 years). The ICER associated with CRT compared to surgery was \$142,883 per life year gained (95% CI \$125,401/life year gained and \$163,449/life year gained), respectively. RT cost more than the other strategies and yielded fewer life years, i.e., RT was dominated by other treatment strategies.

DISCUSSION

This is the first study to evaluate the clinical and economic outcomes of treating T1N0 anal canal cancer by comparing the alternatives of surgery/ablation, CRT, and RT. We found that there was no statistically significant difference in overall survival (both unadjusted and when adjusted using propensity scores) among patients who were treated using surgery/ablation versus those treated with radiotherapy alone or chemoradiotherapy.

When we estimated cost-effectiveness of treatment alternatives using lifetime treatment costs and mean survival time, we found that RT was associated with higher costs and conferred fewer average life years than CRT and surgery did. This trend (i.e., higher cost of RT compared to CRT) might have occurred due to higher cost associated with subsequent recurrence in patients undergoing RT only.²⁴ This possible rationale was based on findings by Zilli et al who found that patients receiving CRT have higher survival when compared with patients receiving RT alone. However locoregional control rates were 100% and 89% in the CRT and radiation-only groups, respectively. We found that when the willingness-to-pay threshold of US\$100,000 per life year (LY)²⁵ is to be considered as the maximum acceptable incremental cost-effectiveness ratio then surgery was considered cost-effective.

To our knowledge, only two previous studies have performed a comparative assessment of the treatments for T1N0 anal canal cancer. In their study, Klas et al. treated 7 patients surgically and 7 patients using a combination modality. The 5-year survival rate in the CRT group was 63% compared with 60% in the surgery group.¹⁴ In 29 patients with T1N0 anal canal cancer, Zilli et al treated 22 patients with CRT and 7 patients with RT only.²⁴ At a median follow-up of 62.5 months, locoregional control was 100% and 89% in the CRT and RT groups, respectively. The 5-year actuarial cancer-specific survival rates for the patients treated with RT alone and CRT were 88.5%±4.5% and 94.9%±2.9%, respectively. In both these studies, it was shown that CRT is associated with better outcomes in terms of 5-year survival than CRT and surgery; however, similar to our analysis, no statistically significant difference was observed due to the small sample size.

Our analysis is the first to report cost-effectiveness for the alternative treatment selection options for T1N0 anal canal tumors. The purpose of cost-effectiveness analysis is estimation

and not hypothesis testing. Thus, ignoring the non-significant association between the treatment strategies, we estimated the incremental cost-effectiveness, where we found that chemoradiotherapy compared to surgery resulted in an ICER of \$142,833/LY gain. When this ICER is compared to the commonly accepted willingness-to-pay threshold of \$100,000/LY gain in the US, CRT would not be considered as a cost-effective strategy.

Our study had several limitations. The retrospective design of our analysis had the limitations inherent to this design. We combined the patients who were treated surgically or using ablation techniques to ensure that we have adequate sample size for the analysis. Since ablation techniques are not currently considered standard of care for invasive anal canal carcinoma, questions may be raised about the appropriateness of the treatment approach in these patients, patient selection and the accuracy of their diagnosis. Furthermore, there are no data on preference-based quality of life or functional outcomes after receiving treatment for anal cancer. Therefore, we did not evaluate clinical outcomes in terms of quality-adjusted life years (QALYs). The results pertain only to patients 66 years or older, and thus cannot be generalized to the overall US population as this population has a higher expected treatment cost owing to more comorbidities when compared with the younger population. Another limitation of our study was the relatively small sample size. We believe that this limitation may have contributed to insufficient statistical power, which could explain in part why none of the relationships in our survival analysis reached statistical significance.

CONCLUSION

Our study is the first to evaluate clinical and economic outcomes associated with T1N0 anal canal cancer treatment. Although the association did not reach statistical significance, we found that patients who were treated surgically might incur less costs, and have similar outcomes to those treated using CRT or RT (i.e., surgery might be a cost-effective use of health care resources). It is crucial to explore this finding further in this era of limited health care resources. The analysis must be revised as more data emerges or outcomes from clinical trials become available. Owing to an increased awareness of cancer screening using anal cytology testing and digital anorectal examination (DARE), more T1N0 anal canal cancers will be diagnosed in the future; therefore, clinical trials evaluating survival, quality of life, and economic outcomes associated with treatment alternatives for T1N0 anal canal cancer are clearly needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

The authors wish to thank Diane Hackett for editorial contributions, which enhanced the quality of the manuscript.

This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors. The authors acknowledge the efforts of the Applied Research Program, NCI; the Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc.; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database.

Role of the funding source: This work was supported by US National Cancer Institute [R01 CA163103], The Janice Davis Gordon Postdoctoral Fellowship in Colorectal Cancer Prevention, and the National Institutes of Health through The University of Texas MD Anderson Cancer Center Support Grant [CA016672], and the Duncan Family Institute.

References

1. Nelson RA, Levine AM, Bernstein L, et al. Changing patterns of anal canal carcinoma in the United States. *J Clin Oncol*. 2013; 31:1569–75. [PubMed: 23509304]
2. American Cancer Society. Survival rates for anal cancer by stage. 2014.
3. Ajani JA, Winter KA, Gunderson LL, et al. US intergroup anal carcinoma trial: tumor diameter predicts for colostomy. *J Clin Oncol*. 2009; 27:1116–21. [PubMed: 19139424]
4. Peiffert D, Tournier-Rangeard L, Gerard JP, et al. Induction chemotherapy and dose intensification of the radiation boost in locally advanced anal canal carcinoma: final analysis of the randomized UNICANCER ACCORD 03 trial. *J Clin Oncol*. 2012; 30:1941–8. [PubMed: 22529257]
5. Epidermoid anal cancer: results from the UKCCCR randomised trial of radiotherapy alone versus radiotherapy, 5-fluorouracil, and mitomycin. UKCCCR Anal Cancer Trial Working Party. UK Coordinating Committee on Cancer Research. *Lancet*. 1996; 348:1049–54. [PubMed: 8874455]
6. Ajani JA, Winter KA, Gunderson LL, et al. Fluorouracil, mitomycin, and radiotherapy vs fluorouracil, cisplatin, and radiotherapy for carcinoma of the anal canal: a randomized controlled trial. *JAMA*. 2008; 299:1914–21. [PubMed: 18430910]
7. Bartelink H, Roelofsen F, Eschwege F, et al. Concomitant radiotherapy and chemotherapy is superior to radiotherapy alone in the treatment of locally advanced anal cancer: results of a phase III randomized trial of the European Organization for Research and Treatment of Cancer Radiotherapy and Gastrointestinal Cooperative Groups. *J Clin Oncol*. 1997; 15:2040–9. [PubMed: 9164216]
8. Flam M, John M, Pajak TF, et al. Role of mitomycin in combination with fluorouracil and radiotherapy, and of salvage chemoradiation in the definitive nonsurgical treatment of epidermoid carcinoma of the anal canal: results of a phase III randomized intergroup study. *J Clin Oncol*. 1996; 14:2527–39. [PubMed: 8823332]
9. Northover J, Glynn-Jones R, Sebag-Montefiore D, et al. Chemoradiation for the treatment of epidermoid anal cancer: 13-year follow-up of the first randomised UKCCCR Anal Cancer Trial (ACT I). *Br J Cancer*. 2010; 102:1123–8. [PubMed: 20354531]
10. Schlienger M, Krzisch C, Pene F, et al. Epidermoid carcinoma of the anal canal treatment results and prognostic variables in a series of 242 cases. *Int J Radiat Oncol Biol Phys*. 1989; 17:1141–51. [PubMed: 2599902]
11. Touboul E, Schlienger M, Buffat L, et al. Epidermoid carcinoma of the anal canal. Results of curative-intent radiation therapy in a series of 270 patients. *Cancer*. 1994; 73:1569–79. [PubMed: 8156483]
12. Peiffert D, Bey P, Pernot M, et al. Conservative treatment by irradiation of epidermoid cancers of the anal canal: prognostic factors of tumoral control and complications. *Int J Radiat Oncol Biol Phys*. 1997; 37:313–24. [PubMed: 9069302]
13. Balamucki CJ, Zlotecki RA, Rout WR, et al. Squamous cell carcinoma of the anal margin: the university of Florida experience. *Am J Clin Oncol*. 2011; 34:406–10. [PubMed: 20881476]
14. Klas JV, Rothenberger DA, Wong WD, et al. Malignant tumors of the anal canal: the spectrum of disease, treatment, and outcomes. *Cancer*. 1999; 85:1686–93. [PubMed: 10223561]
15. Engstrom PF, Arnoletti JP, Benson AB 3rd, et al. NCCN clinical practice guidelines in oncology. Anal carcinoma. *J Natl Compr Canc Netw*. 2010; 8:106–20. [PubMed: 20064293]
16. Warren JL, Klabunde CN, Schrag D, et al. Overview of the SEER-Medicare data: content, research applications, and generalizability to the United States elderly population. *Med Care*. 2002; 40:IV–3–18.
17. Brown ML, Riley GF, Schussler N, et al. Estimating health care costs related to cancer treatment from SEER-Medicare data. *Med Care*. 40:IV–104–17. 2002.
18. Allison, PD. *Survival Analysis Using SAS A Practical Guide* (ed Second Edition). SAS Institute Inc.; Cary, NC: 2012.

19. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. *Biometrika*. 1983; 70:41–55.
20. Cochran WG. The effectiveness of adjustment by subclassification in removing bias in observational studies. *Biometrics*. 1968; 24:295–313. [PubMed: 5683871]
21. Austin PC. An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies. *Multivariate Behav Res*. 2011; 46:399–424. [PubMed: 21818162]
22. Hoch JS, Dewa CS. Advantages of the net benefit regression framework for economic evaluations of interventions in the workplace: a case study of the cost-effectiveness of a collaborative mental health care program for people receiving short-term disability benefits for psychiatric disorders. *J Occup Environ Med*. 2014; 56:441–5. [PubMed: 24662952]
23. Hoch JS. Improving efficiency and value in palliative care with net benefit regression: an introduction to a simple method for cost-effectiveness analysis with person-level data. *J Pain Symptom Manage*. 2009; 38:54–61. [PubMed: 19615627]
24. Zilli T, Schick U, Ozsahin M, et al. Node-negative T1-T2 anal cancer: radiotherapy alone or concomitant chemoradiotherapy? *Radiother Oncol*. 2012; 102:62–7. [PubMed: 21993403]
25. Neumann PJ, Cohen JT, Weinstein MC. Updating cost-effectiveness--the curious resilience of the \$50,000-per-QALY threshold. *N Engl J Med*. 2014; 371:796–7. [PubMed: 25162885]

Figure 1. Flowchart of patient selection

The starting cohort and patient selection criteria is depicted in this figure. After applying the patient selection criteria, a sample of 190 patients was identified for the analysis.

Figure 2. Kaplan-Meier Survival Curves comparing treatment alternatives for T1N0 anal cancer

This figure depicts Kaplan-Meier survival curves for treatment alternatives of surgery (green), radiotherapy (red), and chemoradiotherapy (blue). As seen in the figure, there was no statistically significant difference in the survival as compared by three curves.

Log rank test,

$P = 0.3186$

CRT = chemoradiotherapy

R = radiotherapy

S = surgery/ablation

Table 1

T1N0 anal canal cancer treatment – univariate analysis

	Surgery/ablation N (%)	Radiotherapy N (%)	Chemoradiotherapy N (%)	P-value *
Total	44 (23.16)	50 (26.32)	96 (50.53)	
Age at diagnosis, y				0.103
66-69	12 (27.27)	Not reported [†]	28 (29.17)	
70-74	12 (27.27)	13 (26.00%)	35 (36.46)	
75-79	Not reported [†]	Not reported [†]	18 (18.75)	
80	Not reported [†]	19 (38.00%)	15 (15.62)	
Mean (SD)	76 (7.23)	77 (7.62)	74 (5.75)	
Median (range)	74 (66 – 98)	77 (66 – 99)	72 (66 – 91)	
Marital Status				0.31
Married	14 (31.82)	16 (32.00)	41 (42.71)	
Unmarried	30 (68.18)	34 (68.00)	55 (57.29)	
Geographic region				0.78
MW and NE	12 (27.27)	Not reported [†]	26 (27.08)	
S, W	32 (72.73)	Not reported [†]	70 (72.92)	
Comorbidity score				0.125
0	27 (61.36)	35 (70.00)	61 (63.54)	
1	12 (27.27)	11 (22.00)	28 (29.16)	
2	Not reported [†]	Not reported [†]	Not reported [†]	

MW, Midwest; NE, Northeast; S, South; W, West

*
p-value is based on chi-square test[†] Values were not reported to maintain patient confidentiality (n < 11)

Table 2

Survival analysis: T1N0 anal canal cancer treatment according to treatment and patient characteristics

	Unadjusted		Adjusted		Propensity adjusted	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR 95% CI	P-value
Treatment						
Surgery/ablation	Ref		Ref		Ref	
CRT	1.433 (0.675 – 3.042)	0.35	1.168 (0.768 – 3.623)	0.20	1.742 (0.793 – 3.829)	0.17
RT	1.836 (0.824 – 4.093)	0.14	2.075 (0.895 – 4.811)	0.09	2.170 (0.923 – 5.101)	0.07
Age at diagnosis, y						
66-69	Ref		Ref		Ref	
70-74	0.813 (0.364 – 1.817)	0.61	0.885 (0.385 – 2.029)	0.77	0.864 (0.380 – 1.964)	0.72
75-79	2.012 (0.921 – 4.393)	0.07	1.845 (0.807 – 4.219)	0.15	1.854 (0.821 – 4.186)	0.14
80	1.779 (0.824 – 3.844)	0.14	1.719 (0.772 – 3.830)	0.18	1.728 (0.796 – 3.754)	0.17
Gender						
Male	Ref		Ref		Ref	
Female	1.161 (0.599 – 2.252)	0.66	1.005 (0.502 – 2.013)	0.99	0.994 (0.490 – 2.016)	0.99
Race/Ethnicity						
White	Ref		Ref		Ref	
Non-white	1.644 (0.827 – 3.268)	0.16	1.407 (0.659 – 3.003)	0.38	1.626 (0.781 – 3.388)	0.20
Marital Status						
Married	Ref		Ref		Ref	
Unmarried	1.730 (0.955 – 3.315)	0.07	1.501 (0.804 – 2.801)	0.20	1.624 (0.870 – 3.030)	0.13
Geographic region						
MW and NE	Ref		Ref		Ref	
SW	0.687 (0.392 – 1.202)	0.19	0.750 (0.414 – 1.360)	0.34	0.778 (0.432 – 1.402)	0.40
Comorbidity score						
0	Ref		Ref		Ref	
1	1.746 (0.973 – 3.208)	0.06	1.481 (0.773 – 2.840)	0.24	1.405 (0.729 – 2.711)	0.31
2	2.465 (1.017 – 5.975)	0.04	2.002 (0.755 – 5.313)	0.17	1.774 (0.640 – 4.921)	0.27

Abbreviations: CRT = chemoradiotherapy; RT = radiotherapy; MW and NE = Midwest and Northeast; SW, Southwest

Table 3

Cost-effectiveness analysis

	Mean lifetime cost (\$)	Mean survival time (years)	ICER (\$/year)
Surgery/ablation	29,210	7.60	--
Chemoradiotherapy	46,350	7.72	142,833 (125,401; 163,449)
Radiotherapy	49,400	7.08	Dominated

Future outcomes were discounted at 3%